Task Force 3: Recipient Guidelines/Prioritization

GILBERT H. MUDGE, MD, FACC, CHAIRMAN, SIDNEY GOLDSTEIN, MD, FACC, CO-CHAIRMAN, LINDA J. ADDONIZIO, MD, FACC, ARTHUR CAPLAN, PHD, DONNA MANCINI, MD, T. BARRY LEVINE, MD, FACC, MALCOLM E. RITSCH, JR., JD, LYNNE WARNER STEVENSON, MD, FACC

The prognosis of end-stage heart disease has been dramatically altered by heart transplantation. Although converting enzyme inhibitors have had an important impact on symptomatic status and modest effect on long-term survival in congestive heart failure, the overall annual mortality rate of class IV congestive heart failure continues to be 30% to 40% (1–5). We can now project that patients who receive a heart transplant have an in-hospital mortality rate of <5%, a 1-year survival rate approaching 85% and survival rates of 75% to 80% 5 years after transplantation (see Task Force 4). Not only is quantity of life prolonged, but quality of life is markedly improved, as will be presented in the next section of this report. The success of heart transplantation has resulted in a critical limitation of donor supply, expanding waiting lists and increasing numbers of new transplant centers. The 5th Bethesda Conference (6) in 1968 predicted the promise and the resultant ethical dilemmas that cardiologists now confront.

Each year approximately 40,000 persons under age 65 die from conditions for which heart transplantation may be indicated (7–11). While patient-specific considerations preclude transplantation in many of these persons, the demand for a heart transplant continues to increase. However, donor supply remains unchanged at about 2,000 annually. Thus, far fewer patients receive a transplant than could benefit. Twice as many patients are currently listed for heart transplantation as will undergo transplantation this year. This limited availability of donor organs raises many clinical and ethical issues about the process of patient selection and allocation. Recipient criteria can vary from center to center, but attempts should be made to ensure consistency in clinical evaluation and objective assessment of maximal benefit to be obtained. Assessment of candidates for transplantation who are already dependent on mechanical or parenteral inotropic support is simply a process by which known contraindications to transplantation are systematically excluded. With the increased acceptance of heart transplantation as a viable treatment modality, many patients are understandably referred earlier in the course of their disease and may be judged not to need transplantation for short-term survival benefit. Thus, it becomes increasingly important to stratify the risk for referred patients. Critical examination of recipient criteria and prioritization should be encouraged in light of all these issues.

Current Medical Indications for Heart Transplantation

The current indications for transplantation have been described as "end-stage heart failure," "class III or IV symptoms" and "failure of maximal medical therapy," which are subjective clinical observations that have received little scrutiny and less objective analysis. Clinicians usually examine clinical factors such as escalating medical requirements or frequent hospitalizations, and list patients for heart transplantation when medical therapy seems doomed.

Ischemic heart disease and idiopathic dilated cardiomyopathy are the primary underlying diseases leading to congestive heart failure severe enough to serve as indications for heart transplantation in adults. Patients with advanced valvular heart disease or congenital heart disease are also sometimes suitable candidates. Patients with hypertrophic cardiomyopathy, active myocarditis, sarcoidosis, amyloidosis and primary unresectable cardiac tumors also have had successful transplantation, although progression of amyloidosis or sarcoidosis may limit the long-term benefit of the procedure (12), and patients with active myocarditis may have a less favorable outcome after transplantation (13). Refractory angina in patients who have undergone repeated revascularization procedures is an emerging new indication for transplantation; although these patients may have symptomatic benefit, there is no current evidence that they have improved survival over that achieved with "maximal" medical therapy. Heart transplantation has been considered in some centers to be a lower risk form of surgical intervention than high risk revascularization procedures or valve replacement and, hence, is recommended to some patients rather than more conventional surgical interventions.

Several well established co-morbid conditions in potential recipients have traditionally served as secondary exclusion

JACC Vol. 22, No. 1
July 1993:1–64

Table 1. Secondary Exclusion Criteria for Heart Transplantation

Coexistent systemic illness with poor prognosis
Irreversible pulmonary parenchymal disease
Irreversible renal dysfunction with serum creatinine >2 mg/dl or creatinine clearance <50 ml/min
Irreversible hepatic dysfunction
Severe peripheral and cerebrovascular obstructive disease
Insulin-dependent diabetes with end-organ damage
Active infection
Coexisting neoplasm
Pulmonary hypertension with irreversibly high pulmonary vascular resistance (pulmonary vascular resistance >6 Wood units or 3.0 Wood units after treatment with vasodilators)
Acute pulmonary embolism or infarction
Active diverticulosis or diverticulitis
Active peptic ulcer disease
Myocardial infiltrative and inflammatory diseases
Severe obesity
Severe osteoporosis
Psychosocial instability or substance abuse, or both

criteria (Table 1) and need to be carefully excluded or evaluated during routine screening (Table 2). Active substance abuse is believed to define a patient group that will do poorly after heart transplantation (14,15). On the basis of some clinical experience, patients with congestive heart failure due to anthracycline cardiotoxicity who are believed to have been cured of malignancy by conventional clinical criteria may be considered for cardiac transplant. Clinically significant cerebral or peripheral vascular disease should be reason for exclusion when its presence limits rehabilitation.

Experience in some centers has challenged many of the listed secondary exclusion criteria for heart transplantation. Diabetic patients without severe secondary end-organ disease (retinopathy, neuropathy or nephropathy) have undergone transplantation successfully with excellent intermediate results (16). Patients with refractory endocarditis have likewise undergone successful transplantation without recurrent infection (17). Current surgical skills and immunosuppressive strategies now permit combined transplantations in some centers for patients with previous absolute contraindications: combined kidney and heart transplantation for renal failure and heart failure, and combined liver and heart transplantation for familial hypercholesterolemia and end-stage coronary artery disease (18). Although such procedures are a testimony to surgical expertise, they also challenge current indications and contraindications for heart transplantation and should only be performed as experimental procedures and not accepted as a standard of care.

Older age has historically been considered among the primary exclusion criteria for transplantation. Early collective transplant experience used the age of 55 years as an upper limit, but more recent experience indicates that highly selected older patients receive the same short-term benefit as younger patients (19). It has been proposed that recipient age be considered a factor in donor allocation (older donor hearts placed in the older recipient), but there continues to be reluctance to add this dimension to a complicated ethical and medical dilemma.

Table 2. Recommended Evaluation Before Transplantation

General data
Comprehensive history and physical examination
Blood chemistry determinations including renal and liver function panels
Complete blood count, differential, platelet count, prothrombin time, partial thromboplastin time, fibrinogen
Urinalysis
Stool for guaiac examination ×3
24 hour collection of urine for creatinine clearance, total protein
Nutritional status and diet history
Mammography*
Papanicolaou smear*
Consultation*
Psychiatry
Physical therapy
Social services
Dental
Pulmonary function testing*
Lung ventilation-perfusion scanning*
Basic cardiovascular data
Electrocardiogram
Chest X-ray film
Exercise test with oxygen consumption (peak VO_2)
Detailed hemodynamic evaluation with right heart cardiac catheterization
Radionuclide ventriculogram*
Echocardiogram
Left heart catheterization*
Myocardial biopsy*
Basic immunologic data
Blood type and antibody screen
Human leukocyte antigen (HLA) typing
Panel of reactive antibodies screen
Basic infectious disease background data
Serology for
Hepatitis HBsAg, HBsAb, HBcAb, C
Herpes group virus
Human immunodeficiency virus
Cytomegalovirus (CMV) IgM and IgG antibody
Toxoplasmosis
Varicella and rubella titers
EB viral capsid IgG, IgM antibodies
Lyme titers*
Histoplasmosis and coccidioidomycosis complement fixing antibodies
Venereal Disease Research Laboratory and fluorescent treponemal antibody tests
Urine for viral cultures (cytomegalovirus, adenovirus)
Throat swab for viral cultures (cytomegalovirus, adenovirus, herpes simplex virus)
Urine culture and sensitivity
Stool for ova and parasites ×3*
Skin testing for purified protein derivative with control, mumps, dermatophytin, histoplasmosis and coccidioidomycosis

*Only if appropriate.

There is one hemodynamic exclusion criterion for orthotopic cardiac transplantation. An elevated pulmonary vascular resistance >6 to 8 Wood units or a transpulmonary gradient >15 mm Hg predicts an individual with a high risk of developing acute right ventricular failure in the immediate

postoperative period as the normal donor right ventricle acutely increases its external work load (20,21). Thus, elevated pulmonary vascular resistance is a primary exclusion criterion for orthotopic transplantation, although heterotopic transplantation or heart-lung transplantation remains a potential option for these patients (22). The pulmonary vascular resistance index (pulmonary vascular resistance corrected by body surface area) may be a better predictor of postoperative right ventricular failure than pulmonary vascular resistance and is most important in pediatric patients (23). It is important that any potential recipient with a marginal pulmonary vascular resistance be assessed with hemodynamic maneuvers that include the administration of nitroprusside, dobutamine, amrinone, prostaglandin E_1 or prostacyclin to demonstrate that the elevated pulmonary vascular resistance either is reversible or will not improve with such intensive medical therapy, making the patient unacceptable as a recipient (24,25). A pulmonary vascular resistance >6 Wood units that decreases by 50% with hemodynamic maneuvers may be acceptable for orthotopic transplantation. Repeat right heart catheterizations may be required serially to assess such favorable changes in pulmonary vascular resistance with continued optimal medical therapy and therefore changing candidacy for orthotopic transplantation.

The psychologic profile is a critical aspect of potential recipient evaluation primarily because of the potential for graft loss due to noncompliance (26). A complete psychosocial evaluation should be performed during the initial evaluation to determine eligibility for transplantation and also to identify potential social and behavioral problems that may require specific intervention before and after transplantation. Potential risk factors for noncompliance include previous substance abuse, mood and personality disorders and inadequate family support. Many patients with severe chronic heart failure will manifest depression, for which evaluation is necessary to distinguish endogenous from exogenous despair and to identify the need for long-term psychiatric therapy after transplantation. Issues of psychiatric diagnoses, societal role and family support can be evaluated primarily in the context of their impact on potential compliance rather than by invocation of societal norms and values. All impaired or disabled patients, whether the disability limits physical or mental performance, should be evaluated on an individual basis in terms of their ability to comply with their medical regimen and to enjoy prolonged survival after transplantation. Current techniques and criteria of psychologic evaluation vary widely among heart transplant programs and standardized evaluations have been suggested but not validated (27–29). Although extensive research needs to be done in this area, some lessons may be derived from the experience with kidney transplantation, in which a pretransplantation history of noncompliance was highly associated with noncompliance after transplantation (30), which has been shown to be the major cause of late graft loss for both kidneys and hearts (31).

Current Medical Indications for Pediatric Heart Transplantation

The evolution and acceptance of the viability of heart transplantation for pediatric patients have been slower than for adult patients. As of January 1992, the International Society for Heart and Lung Transplantation Registry has recorded 1,430 heart transplant procedures performed in 1,386 children between birth and 18 years of age. Two hundred twenty-five of these procedures were performed in 1989 alone, with almost half of the recipients <10 years of age (32). Although the annual total of adult heart transplant procedures has seemingly leveled off for the past several years, presumably for lack of donor organs, the number of pediatric transplant procedures has continued to increase. Pediatric heart transplantation now comprises 10% of all heart transplantations performed each year.

Heart transplantation is indicated in any child with end-stage heart disease whose condition is refractory to maximal medical therapy and for whom there is no available surgical procedure that could reasonably restore the patient to a productive life. The two main diagnoses leading to the need for heart transplantation in infants and children are cardiomyopathy and complex congenital heart disease with or without myocardial failure. Although there are still more pediatric patients who have received their transplant because of end-stage cardiomyopathic processes than for other reasons, the pattern of diagnoses for which transplantation has been performed has changed over the past 10 years. With improved surgical techniques and perioperative immunosuppressive management, the number of patients with complex congenital heart lesions undergoing transplantation as a primary or salvage procedure has steadily increased; this, in part, explains the increasing number of children undergoing transplantation before 1 year of age. As of 1989, congenital heart disease was the most common indication for transplantation in pediatric patients.

In pediatric patients, the natural history of heart failure syndromes is not precisely defined. Although most cardiologists would agree that a child with end-stage heart failure who requires inotropic support should be evaluated for transplantation, the progression of disease in children with heart failure who are not yet hospital bound can be very unpredictable. There is no consensus of reliable predictors for poor survival in dilated cardiomyopathy or heart failure in children (33,34). As in adults, significant arrhythmias and high filling pressures have been identified as possible predictors of early mortality and may serve to identify a subgroup that would benefit from urgent transplantation.

Despite the emergence of possible prognostic factors in heart failure syndromes, each patient is different, and all the clinical information on each must be considered before the decision is made to proceed with transplantation. Some children with unmeasurable ventricular function may be surprisingly free of symptoms and may do well for years until a viral illness compromises the remaining cardiac

JACC Vol. 22, No. 1
July 1993:1–64

reserve. General clinical indications for referral to a transplant program include increasing congestive failure despite maximal dosage of oral diuretic agents and afterload reduction with an angiotensin-converting enzyme inhibitor. Congenital heart lesions must be evaluated in the context of their physiology; in some cases, poor ventricular function will not be the reason for referral for transplantation. For example, in patients with a single ventricle after performance of a Fontan repair, only mildly depressed systemic ventricular function in addition to an abnormality in lung perfusion could be responsible for low output and make transplantation the only option for survival. Other clinical indications for transplant evaluation include growth failure or cardiac cachexia, even when control of symptomatic congestive heart failure appears adequate.

Although most of the established exclusionary comorbidities in adult recipients apply to pediatric patients, a few are modified and some are unique. Significant irreversible hepatic or renal dysfunction or infection remains a contraindication to transplantation. Prior strokes or seizure disorders are not exclusionary if the outlook for recovery of function is reasonable. Systemic diseases that preclude transplantation encompass such disorders as degenerative neuromuscular diseases or neoplasia. One challenging aspect of transplantation in children involves reconstruction of complex congenital lesions and the creative surgical approaches that must be devised to repair them. It has been shown that virtually any anatomic aberration of arterial or venous connection is surmountable with heart transplantation except when the pulmonary arteries are too small to be repaired; the patient with inadequate pulmonary artery diameter at the hila should not be considered a candidate for an orthotopic transplant, but would need heart-lung transplantation (35,36).

With the refinement of fetal echocardiography, there is now a new subset of potential patients with lethal cardiac anomalies who are being considered for transplantation while still in utero. When feasible, the delivery of the infant is coordinated with donor procurement. The in utero evaluation of these patients consists of accurate diagnosis, exclusion of other anatomic and medical contraindications and family counseling. The United Network for Organ Sharing (UNOS) has a special category for listing these potential patients after 32 weeks' gestation so that they will not take precedence over neonates already listed (37).

Another criterion unique to transplantation in children is the demonstration of a reliable caregiver for the dependent child. Intensive education of the family as to the lifestyle, risks and complications that can accompany transplantation is essential. A pediatric transplant program has the obligation to seek a competent caregiver when one is not readily obvious. The caregiver identified need not be a parent; however, he or she must have legal responsibility for total care in order to deal with the strict medical regimen required for these patients. This criterion is equally important for the adolescent patient because of the propensity for noncompliance in this age group. Another unique feature is that the pediatric cardiac transplant recipient pool is still small compared with the number waiting for adult donors. Some donor organs are discarded or used for homografts when there is no available recipient for small-sized donors. It is reasonable to offer transplantation and a lower but significant chance for survival to these very high risk children when a donor heart cannot be used for a more suitable candidate.

Table 3. Potentially Reversible Conditions Contributing to Heart Failure Decompensation

Patient-specific considerations
Recent onset of nonischemic cardiomyopathy
Major areas of reversible myocardial ischemia
Atrial fibrillation or other atrial arrhythmias
Alcohol consumption
Endocrine disorders
Physician- and nurse-specific considerations
Perception of "failure of medical therapy"
Inadequate recognition of volume overload
Ineffective use of vasodilators and diuretic agents
Therapy with negative inotropic drugs
Therapy with prostaglandin inhibitors
Lack of patient education about compliance regarding salt, fluid and diuretic adjustment

Limitations of Current Medical Indications

Discussions about patient selection for transplantation have previously focused on the contraindications rather than on objective indications. Before examining these objective indications for transplantation, there are several general clinical considerations that should be emphasized regarding the importance of the careful initial evaluation and ongoing reevaluation by transplant centers of patients selected for heart transplantation.

1. Every patient, regardless of the nature and degree of cardiac dysfunction, deserves evaluation for the potentially reversible factors contributing to decompensation (Table 3). The intensity of this component of the evaluation varies considerably among transplant programs. Common factors limiting adequate compensation of heart failure include atrial fibrillation, subtherapeutic use of diuretics and vasodilators and incomplete patient education about how to monitor and control volume status. Adequate therapy may be prevented by lack of clinical recognition of hypervolemia, fear of potential hypovolemia and concerns about the danger of hypoperfusion with the use of low dose converting enzyme inhibitor (38,39).

2. Present extended waiting times allow for clinical improvement to occur before transplantation; the condition of many patients may be stabilized on medical therapy and transplantation can be safely deferred (40). Frequently the referring physicians and patient will focus on the transplant process once it has been activated and may be reluctant to consider medical therapy even if stability or improvement is

documented (41). In the face of this pressure, there has been no systematic approach to reevaluation of those outpatients who remain on the list for extended periods of time, often over a year, and "de-listing" of an accepted recipient who has had fortunate clinical improvement is rare. De-listing of those stable patients will only be feasible and ethical and have an impact on the prolonged waiting list if it is done on a consistent basis by *all* transplant centers utilizing objective criteria to be further discussed and if the ultimate priority of the deselected patient, if relisted, is further defined by UNOS.

There has also been insufficient emphasis on the continued observation of patients initially considered not to need transplantation at the time of initial evaluation. In one study (40), 40% of such patients died within a year after returning to their communities without provision for expert systematic reassessment. This study provides evidence for the need for expert periodic and objective reassessment by qualified transplant centers of all patients initially considered to be too well to be listed for transplantation.

3. The length of current waiting lists and prioritization schemes are evidence that current medical indications for listing potential recipients do not provide an objective assessment of prognosis. In addition to the 2,500 patients currently listed for heart transplantation in the U.S., 300 more are added each month. Only 150 will receive a transplant each month. Patients in critical condition are first to receive a transplant under present allocation systems, and they make up only 5% to 6% of the total waiting list at any given time. Approximately 20% of candidates who are initially listed as critical will not survive to transplantation. In contrast, the condition of <20% of the patients initially listed as outpatients will become critical in the 1st year after listing. However, >50% of patients currently listed will survive for an extended period outside the hospital without transplantation (42). Although it is difficult to estimate candidate survival without transplantation because of the frequency of transplantation, in one study actuarial survival without transplantation in a stable group of outpatients was 67% at 1 year. For those who survived 6 months on the waiting list, survival over the next 12 months was 83% when careful management was continued. For those patients who survive 9 months waiting for a transplant, transplantation does not appear to convey an additional short-term survival benefit over the next year (42). These patients should probably not continue to be listed for transplantation. All transplant programs should continuously screen waiting lists to ensure that the active list represents a patient group with maximal benefit for survival with transplantation.

4. Given the limited donor supply, objective recipient criteria should be developed to maximize the benefit offered by heart transplantation. This problem becomes more focused if we evaluate patients and estimate benefits for only 1 year at a time. Patients with a poor 5-year prognosis may have a good prognosis for 1 year, after which they should again be evaluated to determine their need for transplantation during the next year. Conversely, patients with recent deterioration may have a poor 1-year prognosis that improves if they are able to achieve and maintain compensation during the next year. The potential impact of decisions based on yearly prognosis is clarified by a computer model simulation of heart transplant candidate pools and risks (43). Utilizing current subjective indications, within 5 years we will reach a candidate pool of almost 4,000 patients; 90% will be outpatients, and only the 300 critically ill candidates in the hospital at any given time will have a chance to receive a heart. Under these conditions, even these critically ill candidates will have only a 50% chance for a heart each month and few outpatients will undergo transplantation. We can also estimate that 50% of outpatients now listed will die suddenly or their condition will deteriorate without transplantation during the next year. If *current* information about risk assessment were applied nationally, the number of outpatients listed probably could be reduced by at least 30%. If this practice were to start in 1993, the waiting list could be reduced to <1,000 within 3 years, even if the number of candidates for urgent transplantation did not change from the current number. Outpatients would then have an average 12% chance of transplantation each month compared with 3% currently, and would less frequently experience deterioration of their condition to require urgent transplantation.

5. Regardless of the etiology of disease or prior history of decompensation, identification of the patient who needs transplantation must focus on the relative prognosis for survival with transplantation versus that with other therapies rather than limitations of functional capacity. Functional capacity will be improved but not restored to completely normal by transplantation; on average, it will be similar to that achieved by patients who have survived with heart failure that is "stable" by clinical criteria: approximately 60% to 70% of normal predicted performance (44). There are some indications that performance of low level exercise consistent with daily activity may improve more than peak capacity (45). Thus, the patient who is in stable condition and comfortable performing routine activities, but "would like to do more" may not necessarily derive benefit from transplantation. With the limited number of donor hearts available, the argument could be made that the overall benefit to patient candidates is maximized by maximizing survival rather than functional capacity, which often deteriorates and improves concomitantly with expected survival. Moreover, heart transplantation should not replace other high risk surgical interventions simply because collective results offer a better long-term survival.

6. It should be emphasized that donor organs are a societal and regional resource that must be allocated in a fair, consistent and equitable fashion. Consistent objective criteria for patient eligibility are necessary to prevent "program shopping" by patients with the resources to do so and "candidate shopping" by programs looking for the lowest postoperative mortality statistics, which may be achieved by performing a transplant procedure in those patients who

JACC Vol. 22, No. 1
July 1993:1–64

need it least. The length of recipient waiting lists is also one of the justifications given for listing patients before severe decompensation, which leads to further list expansion and yet longer waiting times. Because many patients await heart transplantation at home, and allocation of hearts is often made solely on the basis of waiting time, this subjective clinical criterion will not identify those persons in greatest need of transplantation.

Indications for Retransplantation

The clinical and ethical issues of retransplantation should also be addressed. Care should be taken that patients do not feel abandoned when retransplantation is not an option. Recurrent rejection and allograft coronary artery disease will inevitably lead to a finite number of graft failures in patients who continue to be suitable candidates for retransplantation without secondary co-morbidity. The ultimate decision regarding the appropriateness of retransplantation should distinguish between retransplantation for acute histologic rejection, which has been associated with a poor short-term prognosis, and retransplantation for allograft coronary artery disease or chronic graft failure, which may have a short-term survival rate comparable to that for initial transplantation in critically ill patients. But because the issue of heart retransplantation is not unique in this era of limited donor supply and restrained financial resources, the entire transplant community must confront the many complicated dilemmas of retransplantation for all solid organs.

General Recommendations for Objective Recipient Criteria

Although it will not be possible to develop perfect objective clinical criteria to identify patients who should and should not be placed on the transplant waiting list, the ability to predict survival in patients with heart failure is critical to optimizing the selection of transplant candidates. In early studies, several univariate predictors of reduced survival in patients with heart failure were identified (45–51). These predictors included a reduced left ventricular ejection fraction, New York Heart Association functional class, the presence of a third heart sound, left ventricular conduction delay on a baseline ECG, reduced serum sodium, elevated serum catecholamines, increased pulmonary capillary wedge pressure, reduced cardiac index and low peak oxygen consumption (VO_2). A few studies have used multivariate techniques to predict survival but no consistent objective clinical criteria have emerged. These early studies may not reflect current medical practice, as antiarrhythmic drug use was more prevalent and use of angiotensin-converting enzyme inhibitors more sparing. Multivariate analysis performed on 15 variables from 1,088 patients enrolled in the recent PROMISE trial may be more reflective of current medical practices. Baseline variables that provided independent prognostic information were nonsustained ventricular tachycardia on 24-hour ambulatory ECG (Holter) monitoring, New York Heart Association functional class, ejection fraction, serum sodium, blood urea nitrogen and antiarrhythmic drug use (52).

Although ejection fraction is the best variable to quantify myocardial failure, it does not quantify the degree of congestive heart failure and it cannot predict the degree of clinical compensation that can be achieved and maintained. Approximately 95% of patients who undergo transplantation have congestive heart failure with a markedly reduced ejection fraction. One prospective analysis (53) of 79 patients with idiopathic dilated cardiomyopathy found ejection fraction to be the sole predictor of survival. The investigators recommended heart transplantation for all patients with an ejection fraction <20%, a recommendation that must be viewed with caution because the statistical analysis is flawed, with no formal testing of difference in survival between subgroups stratified by ejection fraction. The number of such patients with a reduced ejection fraction not only exceeds the number of available hearts but, if these patients are discharged from the hospital, they can have a 1-year survival rate without transplantation that is 60% and even higher in some subgroups (54).

The other clinical criteria for patients with more advanced heart failure—New York Heart Association functional class III or IV, history of frequent hospitalizations, high pulmonary artery wedge and right atrial pressures, low cardiac output, low serum sodium, elevated plasma norepinephrine levels, history of syncope, symptomatic ventricular arrhythmias and sudden death—all identify patients who need further therapy but not necessarily transplantation. Each of these clinical variables has usually been measured at peak decompensation and may be of more prognostic value in this group if they are assessed after maximal medical interventions. Most important, there are no currently validated indexes of prognosis that are not heavily influenced by the adequacy of therapy immediately before evaluation.

Once maximal therapy has been instituted and maintained, peak VO_2 measured during maximal exercise testing provides an objective assessment of functional capacity in patients with heart failure and an indirect assessment of cardiovascular reserve. The value of peak VO_2 in optimally timing heart transplantation was studied in 114 consecutive ambulatory patients referred for heart transplantation evaluation between 1986 and 1989 (55). Patients were prospectively classified into three groups: Group 1 patients had peak VO_2 ≤14 ml/kg per min and were accepted as transplant candidates; Group 2 patients had peak VO_2 >14 ml/kg per min and transplantation was deferred; Group 3 patients had peak VO_2 ≤14 ml/kg per min but were rejected for transplantation for noncardiac reasons. Serial assessments were performed with crossover between Groups 1 and 2. The three groups had comparable functional class, left ventricular ejection fraction and cardiac index. Patients with VO_2 >14 ml/kg per min had a 1-year survival rate of 94%,

confirming that heart transplantation could be safely deferred. The major risk to these patients was that of sudden death.

The worst survival rates occurred in those candidates with peak VO_2 ≤10 ml/kg per min. All such patients should be accepted as transplant candidates in the absence of contraindications. In many patients with peak VO_2 >14 ml/kg per min, transplantation may be deferred, unless other clinical features such as symptomatic ventricular arrhythmias, intractable myocardial ischemia and persistent fluid retention are identified.

In patients with VO_2 ≤14 ml/kg per min, it is important to establish that exercise testing was truly maximal. Achievement of anaerobic metabolism should be identified in all patients at roughly 50% to 70% peak VO_2 unless the test is terminated early by ischemia. Though peak VO_2 provides an indirect assessment of cardiac output and cardiac reserve, a variety of factors serve to limit peak VO_2. These include age, gender, conditioning status, muscle mass and angina. A peak VO_2 of 14 ml/kg per min represents approximately 60% of predicted maximal exercise capacity for an active 60-year old man but only 30% of the predicted capacity for a 20-year old man. This level of activity may provide an unacceptable quality of life for a young adult. Peak VO_2 is a powerful criterion that needs to be viewed in the context of the total evaluation procedure *and* the patient's age. The ability to demonstrate an improvement in exercise capacity with medical therapy may be particularly favorable as an indication of restored compensation that will reflect not only an improved prognosis, but also an improved quality of life. The importance of peak VO_2 mandates that it be measured precisely and not estimated by exercise duration or metabolic equivalents (56).

Risk factors less directly related to the degree of hemodynamic compensation have not been well studied. The major threat to survival in patients with preserved exercise capacity is sudden death. Patients with chronic heart failure are at greater risk for sudden death than is any other definable subset of patients in cardiovascular medicine, but our ability to identify those patients with heart failure at greatest risk for sudden death is poor. Poor hemodynamic measurements and the existence of nonsustained ventricular tachycardia do predict total cardiac mortality but not specifically sudden death probability. Electrophysiologic testing, signal-averaged electrocardiography and autonomic profiling have been variably predictive of future fatal arrhythmic events. More investigations are needed to identify patients who are at the greatest risk for sudden death (57).

Summary of General Recommendations

Before assessment of functional status, patients with heart failure should undergo aggressive therapy with combinations of vasodilators and diuretic agents. Therapy should be adjusted until clinical congestion has been resolved or until further therapy has been repeatedly limited by severe hypotension (generally systolic blood pressure <80 mm Hg) or marked azotemia. Patients should not be considered to have *refractory* hemodynamic decompression until therapy with intravenous followed by oral vasodilators and diuretic agents has been pursued using continuous hemodynamic monitoring to approach hemodynamic goals. Once reversible factors of decompensation and the adequacy of medical therapy have been thoroughly addressed, exercise capacity should be assessed by direct measurement of peak VO_2 and compared with that of age-matched normal subjects.

After detailed and expert evaluation, all potential recipients can be considered in one of the three following groups:

I. *Accepted Indications for Transplantation*
   1. Maximal VO_2 <10 ml/kg per min with achievement of anaerobic metabolism
   2. Severe ischemia consistently limiting routine activity not amenable to bypass surgery or angioplasty
   3. Recurrent symptomatic ventricular arrhythmias refractory to *all* accepted therapeutic modalities

II. *Probable Indications for Cardiac Transplantation*
   1. Maximal VO_2 <14 ml/kg per min and major limitation of the patient's daily activities
   2. Recurrent unstable ischemia not amenable to bypass surgery or angioplasty
   3. Instability of fluid balance/renal function not due to patient noncompliance with regimen of weight monitoring, flexible use of diuretic drugs and salt restriction

III. *Inadequate Indications for Transplantation*
   1. Ejection fraction <20%
   2. History of functional class III or IV symptoms of heart failure
   3. Previous ventricular arrhythmias
   4. Maximal VO_2 >15 m/kg per min without other indications

Recipient Priority for Heart Transplantation

Current Status of Priority

The current means of recipient categorization in the U.S. includes an estimation of the recipient's severity of illness and determination of ABO blood type, body size and length of time on the waiting list. Because of the expanding number of recipients, the primary determinants of organ allocation have come to be severity of illness and time on the waiting list. The physically small adult recipient or recipients in AB or B blood groups will usually be on a smaller waiting list, but donor availability is also limited for these patients. Current prioritization systems include a local allocation system and a national listing, both of which are supervised by UNOS. Local organ procurement organizations will allocate the donated organs to all locally listed recipients according to UNOS-approved allocation policies before

JACC Vol. 22, No. 1
July 1993:1–64

Table 4 Current Recipient Status Criteria of the United Network for Organ Sharing (UNOS)

Status I
Patients who require cardiac and/or pulmonary assistance with one or more of the following devices:
(i) Total artificial heart
(ii) Left and/or right ventricular assist systems
(iii) Intra-aortic balloon pump
(iv) Ventilator
Or, patients meeting BOTH of the following criteria:
(i) Patient in an intensive care unit and
(ii) Patient *requires* inotropic agents to maintain adequate cardiac output
Or, patients less than six months old
Status II
All other waiting patients who do not meet the Status I criteria

*UNOS Executive Order, June 24, 1992.

these organs become available for more general distribution according to UNOS national prioritization rules. Highest priority is given to those patients whose condition is considered urgent, or status I, a classification limited strictly to patients in an intensive care unit who are dependent on intravenously administered inotropic agents or on a mechanical support device. All other patients, whether in or out of the hospital, are considered to be in status II (Table 4). The general rationale for such a simplified two-status system was an attempt to instill some degree of accountability for each transplant institution, the assumption being that intensive care units would not be improperly utilized to modify a patient's priority. Many organ procurement organizations have successfully applied for local allocation "variances," that allow for an intermediate status, characterized in most cases by heart failure that requires hospitalization without intensive care, low dose inotropic support not administered in an intensive care unit setting, unstable angina or persistent life-threatening arrhythmias.

The patient's time on the waiting list is the second most important factor in allocation, and begins with the date the patient is entered on the transplant waiting list. According to UNOS guidelines, waiting time is not accrued on a national basis when patients are temporarily listed in an inactive status, but local recipients may return to their original listing date if they have been temporarily classified as inactivated because of intercurrent complications. Although there is a current means of classifying a patient with intercurrent illness as inactivated, there is no systematic and uniformly applied means of so classifying the patient whose condition stabilizes on medical therapy, without jeopardizing their previously accrued waiting time. Finally, logistic issues of transportation have been addressed by UNOS, (Table 5) but because of the number of transplant programs and large regional waiting lists, these logistic considerations are of minimal importance for most critically ill candidates. There continues to be controversy as to whether organs should be distributed according to program or patient location.

Limitations of Current Recipient Prioritization

There is widespread concern over inequity in identifying patients who "urgently" require transplantation. Programs with underutilized or strategically enlarged intensive care unit facilities are more likely to board patients with severe heart failure on inotropic support and allow earlier transplantation. Nursing protocols at some institutions may require low dose inotropic agents to be administered in an intensive care unit setting, enhancing a patient's priority without attendant change in clinical status. In other cases, patients legitimately appearing to be in critical condition may show improvement over time and no longer need urgent transplantation but they continue to be listed at a high priority. These practices may penalize patients who receive diligent care that leads to hospital discharge, prevents future hospitalizations and may also lead to better results after transplantation.

Priority for critically ill patients has also been challenged because such patients have a higher overall mortality rate after transplantation and currently have the highest priority. Although some individual centers have reported equivalent survival data for critically ill and noncritically ill patients, the International Registry demonstrates an operative mortality rate of 14% for critically ill patients compared with 6% for those in stable condition. If the candidate population is considered as a whole, survival *after* transplantation is maximized by performing transplantation only in the healthier outpatients. However, survival for the entire recipient pool should be maximized by performing transplantation first in the patients most likely to die without transplantation, as shown in a computer model constructed using current data for waiting list death, deterioration and posttransplantation mortality for regular and critical status candidates (43). In this model the benefit of giving priority to the sicker patients would be preserved unless their posttransplant mortality rate approached 50%. It is important to recognize that the current priority system does maximize survival for critically ill patients initially listed as outpatients, because the condition of some of these will deteriorate to the point of requiring urgent transplantation as class I priority.

Priority for outpatients of similar size and blood grouping is currently based solely on waiting list time. The immediate impact of this policy is to select patients who have demonstrated survival without transplantation. A subgroup of outpatients who can survive without transplantation for 6 months (the current average waiting time) has an expected survival rate of 83% over the next 12 months, which is comparable to that after transplantation. Within the next 5 years the cumulative effect of our current listing and priority policy is that the number of outpatient candidates will expand to >4,000 whereas hearts will go only to patients whose condition has so deteriorated that they are in-hospital candidates for urgent transplantation.

Table 5. Current Allocation Criteria of the United Network for Organ Sharing (UNOS)*

Local Allocation of Hearts: Hearts will be allocated locally in the following sequence. For every thoracic organ donor, the choice will be made locally whether to use the heart for a heart (without lung) transplant for a Status 1 patient, or for a heart-lung combination transplant. If the heart is to be used for a heart (without lung) transplant, the heart will be allocated first to local Status 1 patients according to length of time waiting. If the organ is not allocated to a Status 1 heart patient, then the heart will be allocated to a local patient awaiting a heart-lung combination transplant who has a blood type that is identical to that of the donor, according to length of time waiting. If the heart is not allocated to a local patient awaiting a heart-lung combination transplant who has a blood type that is identical to that of the donor, then the heart will be allocated to local patients awaiting heart-lung combination transplantation who have a blood type that is compatible with that of the donor, according to length of time waiting. If the heart is not allocated to a Status 1 heart patient or a heart-lung patient, then the heart is allocated to a local Status 2 (ABO identical) patient according to length of time waiting, then to a local Status 2 (ABO compatible) patient according to the length of time waiting.

Local Conflicts: Regarding allocation of hearts, lungs, and heart-lung combinations, locally unresolved inequities or conflicts that arise from prevailing OPO boundaries or policies may be submitted to any interested local member for review and adjudication to the UNOS Thoracic Organ Transplantation Committee, Organ Procurement and Distribution Committee and Board of Directors.

National Allocation: If the heart is not allocated locally, it will be allocated in the following numerical sequence according to the length of time waiting.

Primary Allocation:

Zone A

1. Status 1 heart (without lung) patient
2. Heart-lung combination patient, ABO identical
3. Heart-lung combination patient, ABO compatible

Zone B

4. Status 1 heart (without lung) patient

Zone B and C

5. Heart-lung combination patient, ABO identical
6. Heart-lung combination patient, ABO compatible

Secondary Allocation:

Zone A

7. Status 2 heart (without lung) patient, ABO identical
8. Status 2 heart (without lung) patient, ABO compatible

Zone B

9. Status 2 heart (without lung) patient, ABO identical
10. Status 2 heart (without lung) patient, ABO compatible

Zone C

11. Status 1 heart (without lung) patient
12. Status 2 heart (without lung) patient, ABO identical
13. Status 2 heart (without lung) patient, ABO compatible

The distance of the recipient hospital from the donor hospital will also be used to prioritize the recipient list for hearts, lungs, and heart-lung combination not used by the local OPO. Three zones will be defined by concentric circles of 500 and 1,000 mile radii with the donor hospital as the center. Zone A will extend to 500 miles. Zone B is defined between 500 and 1,000 miles. Zone C is defined as beyond 1,000 miles.

*UNOS Executive Order, June 24, 1992. OPO = organ procurement organization.

Summary of Recommendations Regarding Indications and Priority

Twenty-five years ago, the 5th Bethesda Conference predicted the dilemmas of recipient evaluation and prioritization that are now emerging. This 24th Bethesda Conference accepts its professional responsibility to provide direction toward maximizing the life-saving potential of heart transplantation. We recommend that the following guidelines be adopted in the care of all patients considered for heart transplantation:

1. The evaluation of end-stage heart disease and selection of patients for potential heart transplantation should be done by a multidisciplinary team with appropriate expertise in management of congestive heart failure and high risk surgical intervention as well as transplantation. Early evaluation by such a team should be encouraged, even if imminent transplantation is not anticipated.

2. The indication for transplantation is end-stage heart disease including heart failure, refractory ischemia and arrhythmias, which have led to unacceptable prognosis for survival and unacceptable disability even after careful consideration of all other medical and surgical therapy.

3. The indication for heart transplantation in pediatric patients includes end-stage heart failure and congenital lesions not amenable to surgical repair.

4. The initial evaluation procedure for the potential transplant candidate should provide each patient with a well defined profile that encompasses recognized prognostic variables that predict survival but defines a single point in time in what is clearly a dynamic process. It is essential to continually address reversible factors of decompensation.

5. Potential recipients should be classified as Group I, II or III, by indication for transplantation. All transplant centers should consider these objective criteria in determining active or inactive status of potential recipients.

6. All waiting candidates should be reevaluated at regular intervals of ≤3 months and undergo formal reevaluation at least yearly whether they are on the transplant list or initially

considered not to need transplantation. The 3-month reevaluation should include at a minimum a detailed history, physical examination and exercise test with peak VO_2 measurement; yearly reevaluations should include a complete reevaluation, including right heart catheterization to measure pulmonary vascular resistance.

7. Patients and their referring physicians should be informed at the time of evaluation that listing is a dynamic state from which a given candidate may be removed and returned as his condition changes. Patients should be classified as on inactive status if their condition improves.

8. Discussions with UNOS should be encouraged to explore means of systematically "de-listing" patients who become clinically stable without jeopardizing their previously accrued waiting time should their condition deteriorate.

9. Collection and application of prospective multicenter data on risks before and after transplantation should be encouraged to ensure that this life-saving resource is optimally utilized.

References

1. The CONSENSUS Trial Study Group: Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS) N Engl J Med 1987; 316:1429–35.
2. Wilson JR, Schwartz JS, St. John Sutton M, et al. Prognosis in severe heart failure: relation to hemodynamic measurements and ventricular ectopic activity. J Am Coll Cardiol 1983;2:403–10.
3. Kriett JM, Kaye MP. The registry of the International Society of Heart Transplantation: Seventh Official Report—1990. J Heart Transplant 1991; 9:232–30.
4. Cohn JN, Johnson G, Ziesche S, et al. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. N Engl J Med 1991;325:303–10.
5. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. N Engl J Med 1991;325:293–302.
6. 5th Bethesda Conference Report: Cardiac and Other Organ Transplantation. Am J Cardiol 1968;22:896–912.
7. Evans RW, Manninen DL, Dong FB. The National Cooperative Transplantation Study: Final Report. Seattle: Battelle Seattle Research Center, 1991.
8. Kottke TE, Pesch DG, Frye RL, et al The potential contribution of cardiac replacement to the control of cardiovascular diseases: a population based estimate. Arch Surg 1990;125:1148–51.
9. Evans RW. Executive summary: The National Cooperative Transplantation Study. Report BHARC-100-91-020. Seattle: Battelle Seattle Research Center, June 1991.
10. Evans RW. Social, economic, and insurance issues in cardiac replacement. In: O'Connell JB, Kaye MP, eds., Intrathoracic Transplantation 2000. Austin, TX: RG Landes, 1993:1–17.
11. Evans RW, Orians C, Ascher NL. The potential supply of organ donors: an assessment of organ procurement effects in the United States. JAMA 1992;267:239–46.
12. Hosenpud JD, Uretsky BF, Griffith BP, O'Connell JB, Olivari M-T, Valantine HA. Successful intermediate-term outcome for patients with cardiac amyloidosis undergoing heart transplantation: results of multicenter survey. J Heart Transplant 1990;9:346–50.
13. O'Connell JB, Dec GW, Goldenberg IF, et al. Results of heart transplantation for active lymphocytic myocarditis. J Heart Transplant 1990;9: 351–6.
14. Holland C, Hagan M, Volkman K, et al. Substance abuse: does this warrant exclusion for transplant (abstr). J Heart Transplant 1988;7:70.
15. Hanrahan JS, Taylor DO, Eberly C, et al. Cardiac allograft survival in "reformed" substance abusers (abstr). J Heart Lung Transplant 1991;10: 158.
16. Munoz E, Lonquist J, Radovancevic B, et al. Long-term results in diabetic patients undergoing cardiac transplantation. J Heart Transplant 1991;10:189–90.
17. DiSesa VJ, Sloss LJ, Cohn LH. Cardiac transplantation for intractable prosthetic valve endocarditis. J Heart Transplant 1990;9:142–3.
18. Gonwa TA, Husberg BS, Klintmatin GB, et al. Simultaneous heart and kidney transplantation: a report of three cases and review of the literature. J Heart Lung Transplant 1992;11:152–5.
19. Olivari MT, Antolick A, Kaye MP, Jamieson SW, Ring WS. Heart transplantation in elderly patients. J Heart Transplant 1988;7:258–64.
20. Griepp RB, Stinson EB, Dong E Jr, Clark DA, Shumway NE. Determinants of operative risk in human heart transplantation. Am J Surg 1971;122:192–7.
21. Kormos RL, Thompson M, Hardesty RL, et al. Utility of preoperative right heart catheterization data as a predictor of survival after heart transplantation (abstr). J Heart Transplant 1986;5:391.
22. Desruennes M, Muneretto C, Gandjbakhch I, et al. Heterotopic heart transplantation: current status in 1988. J Heart Transplant 1989;8: 479–85.
23. Addonizio LJ. Cardiac transplantation in the pediatric patient. Prog Cardiovasc Dis 1990;33:19–34.
24. Costard-Jackle A, Fowler MB. Influence of preoperative pulmonary artery pressure on mortality after heart transplantation: testing of potential reversibility of pulmonary hypertension with nitroprusside is useful in defining a high risk group. J Am Coll Cardiol 1992;19:48–54.
25. Murali S, Uretsky BR, Armitage JM, et al. Utility of prostaglandin E-1 in the pretransplant evaluation of cardiac failure patients with significant pulmonary hypertension. J Heart Lung Transplant 1992;11:716–23.
26. Mai FM, McKenzie FN, Kostuk WJ. Psychiatric aspects of heart transplantation: preoperative evaluation and postoperative sequelae. Br Med J 1986;292:311–3.
27. Freeman AM, Folks DG, Sokol RS, Fahs JJ. Cardiac transplantation: clinical correlates of psychiatric outcome. Psychosomatics 1988;29: 47–50.
28. Olbrisch ME, Levenson JL, Hamer R. The PACT: a rating scale for the study of clinical decision-making in psychosocial screening of organ transplant candidates. Clin Transplant 1989;3:164–9.
29. Olbrisch ME, Levenson JL. Psychological evaluation of heart transplantation candidates: an international survey of process, criteria, and outcomes. J Heart Lung Transplant 1991;10:948–55.
30. Rodriguez MD, Colon A, Santiago-Delphin EA. Psychosocial profile of noncompliant patients. Transplant Proc 1991;23:1807–9.
31. Rovelli M, Palmeri D, Vossler E, Bartus S, Hull D, Schweizer R. Noncompliance in organ transplant recipients. Transplant Proc 1989;21: 833–4.
32. Kaye MP. The Registry of the International Society for Heart and Lung Transplantation. Ninth Official Report. J Heart Lung Transplant 1992;11: 599–606.
33. Lewis AB, Chabot M. Outcomes of infants and children with dilated cardiomyopathy. Am J Cardiol 1991;68:365–9.
34. Addonizio LJ. Cardiac transplantation for cardiomyopathies of childhood. Prog Pediatr Cardiol 1992;1:72–80.
35. Cooper MM, Fuzesi L, Addonizio LJ, Hsu DT, Smith CR, Rose EA. Pediatric heart transplantation following surgery involving the pulmonary arteries. J Thorac Cardiovasc Surg 1991;1:386–95.
36. Michler RE, Smith CR, Quaegebeur JM, Hsu DT, Addonizio LJ, Boxt L, Rose EA. Surgical lessons learned in heart transplantation for complex congenital heart disease. J Thorac Cardiovasc Surg (in press)
37. United Network for Organ Sharing, Policy 3.2.1.6; June 24, 1992.
38. Stevenson LW. Tailored therapy before transplantation for treatment of advanced heart failure: effective use of vasodilators and diuretics. Heart Lung Transplant 1991;10:458–76.
39. Stevenson LW, Miller L. Cardiac transplantation as therapy for heart failure. Curr Prob Cardiol 1991;16:4:219–305.
40. Stevenson LW, Fowler MB, Schroeder JS, Stevenson WG, Dracup KA, Fond V. Poor survival of patients with idiopathic cardiomyopathy considered too well for transplantation. Am J Med 1987;83:871–6.

41. Caplan AL. If I Were A Rich Man Could I Buy a Pancreas? Indiana University Press, 1992.
42. Stevenson LW, Hamilton MA, Tillisch JH, et al. Decreasing survival benefit from cardiac transplantation for outpatients as the waiting list lengthens. J Am Coll Cardiol 1991;18:919–25.
43. Stevenson LW, Warner SL, Hamilton MA, et al. Distribution of donor hearts to maximize transplant candidate survival. Circulation 1991; 84(suppl II):II-352.
44. Stevenson LW, Sietsema K, Tillisch JH, et al. Exercise capacity for survivors of cardiac transplantation or sustained medical therapy for stable heart failure. Circulation 1990;81:78–85.
45. Chelimsky-Fallick C, Stevenson LW, Whipp B, Lem V. Normalization of oxygen deficit in low-level exercise may explain major functional improvements after cardiac transplantation (abstr). J Heart Lung Transplant 1992;11:203.
46. Gradman A, Deedwania P, Cody R, Massie B, Packer M, Pitt B. Predictors of total mortality and sudden death in mild to moderate heart failure. J Am Coll Cardiol 1989;14:564–70.
47. Cohn JN, Archibald DG, Francis GS, et al. Veterans Administration Cooperative Study on Vasodilator Therapy of Heart Failure: influence of prerandomization variables on the reduction of mortality by treatment with hydralazine and isosorbide dinitrate. Circulation 1987;75(suppl IV): IV-49–54.
48. Franciosa JA, Wilen M, Ziesche S, Cohn JA. Survival in men with severe chronic left ventricular failure due to either coronary artery disease or idiopathic dilated cardiomyopathy. Am J Cardiol 1983;51:831–6.
49. Unverferth DV, Magorien RD, Moeschberger ML, Baker PB, Fetters JK, Leier CV. Factors influencing the one-year mortality of dilated cardiomyopathy. Am J Cardiol 1984;54:147–52.
50. Cohn JN, Levine TB, Olivari MT, et al. Plasma norepinephrine as a guide to prognosis in patients with chronic congestive heart failure. N Engl J Med 1984;311:819–23.
51. Lee W, Packer M. Prognostic importance of serum sodium concentration and its modification by converting enzyme inhibition in patients with severe heart failure. Circulation 1986;73:257–67.
52. Mancini DM, Benotti JR, Cheseboro JH, et al. Antiarrhythmic drug use and high serum levels of digoxin are independent adverse prognostic factors in patients with chronic heart failure. Circulation 1991;84(suppl II):II-243A.
53. Keogh AM, Baron DW, Hickie JB. Prognostic guides in patients with idiopathic or ischemic dilated cardiomyopathy assessed for cardiac transplantation. Am J Cardiol 1990;65:903–8.
54. Stevenson LW, Tillisch JH, Hamilton M, Luu M, Chelimsky-Fallick C, Moriguchi J, Walden J. Importance of hemodynamic response to therapy in predicting survival with ejection fraction ≤20% secondary to ischemic or non-ischemic dilated cardiomyopathy. Am J Cardiol 1990;66: 1348–54.
55. Mancini DM, Eisen H, Kussmaul W, Mull R, Edmunds LH, Wilson JR. Value of peak exercise oxygen consumption for optimal timing of cardiac transplantation in ambulatory patients with heart failure. Circulation 1991;83:778–86.
56. Kermani M, Stevenson LW, Chelimsky-Fallick C, et al. Importance of serial exercise testing after evaluation for cardiac transplantation. J Heart Lung Transplant 1992;11:191.
57. Mancini DM, Wong KL, Simson MB. Prognostic value of an abnormal signal-averaged electrocardiograms in patients with nonischemic congestive cardiomyopathy. Circulation 1993;87:1083–92.

Task Force 4: Function of the Heart Transplant Recipient

JAMES B. YOUNG, MD, FACC, CHAIRMAN, WILLIAM L. WINTERS, JR., MD, FACC, CO-CHAIRMAN, ROBERT BOURGE, MD, FACC, BARRY F. URETSKY, MD, FACC

Introduction

Heart transplantation affords a remarkable degree of rehabilitation for patients with end-stage heart failure and all of its attendant hemodynamic abnormalities and functional limitations. In highly selected patients this surgical procedure is vastly superior to other existing forms of therapy in improving functional capacity and survival. Cardiac allografts, however, do not function totally normally and exercise tolerance in transplant recipients is somewhat less than might be expected. It is important to understand the implications of the altered physiology of the denervated heart because of its relation to exercise tolerance, physical rehabilitation, postoperative complications and pharmacotherapeutic intervention.

Heart transplant recipients often have severe psychologic dysfunction caused by symptoms from their previous cardiac disease, the stresses imposed by these symptoms and concern regarding impending death. In most cases, heart transplantation results in resolution or marked improvement of cardiovascular symptoms and anticipated survival. Therefore, exploring quality of life after transplantation also is important.

Physiology

The function of the orthotopically transplanted heart is a complicated interplay of ventricular loading conditions, intrinsic myocardial contractile capability, circulating catecholamine levels, denervation (with, in some cases, partial reinnervation), donor/recipient size relation, pulmonary performance and atrial function. Table 1 summarizes many of the issues relevant to function of the transplanted heart.